

WHERE ANGELS FEAR TO TREAD: DVT & LOW MOLECULAR WEIGHT HEPARIN

A number of *Bandolier's* readers have asked *Bandolier* to report on the use of low molecular weight heparins in the prevention and treatment of deep vein thrombosis (DVT). This is one of those topics where there seems to be much nuance and some major disagreements. It is one of those areas where angels fear to tread.

The safe way to seek to illuminate the subject, therefore, is to stick with evidence of high quality - from systematic reviews and meta-analyses of randomised controlled trials (see *Bandolier* #12).

Last month (*Bandolier* #16) we reported on a systematic review and meta-analysis of graduated compression stockings and DVT. This showed that the prophylactic use of stockings in moderate risk surgery resulted in a reduction in risk of DVTs by 68% and had a NNT of 9 (7 - 13) compared to no treatment. The low molecular weight heparins pose a somewhat different problem - but this month we examine some work on these for comparison.

This leads to the question of what happens if both low molecular weight heparins and compression stockings are used. Right now *Bandolier* has not found any information about that, but we would be delighted if any reader could uncover suitable reviews of RCTs on this question.

How much controversy is there in this area? We would welcome any evidence-based correspondence - perhaps pointing to the successful use of audit to change practice, or evidence that preventing DVTs confers long term health and economic benefit.

Low molecular weight heparins

There are two systematic reviews which may be useful to readers and institutions trying to develop policy in this area. One is a study of the use of low molecular weight heparins (LMWH) in the prevention of deep vein thrombosis (DVT) in total hip replacement [1], and the other investigates the effects of LMWH in treating such events [2].

PREVENTION

From McMaster University comes a report of the use of LMWH in prevention [1]. Randomised controlled trials (RCTs) which compared LMWH directly with standard

heparins in total hip replacement were sought - six were found.

Outcome measures

The principal outcome measure was total DVT incidence. This was subdivided into proximal (popliteal or more proximal leg veins) or distal (isolated deep veins of the calf) events. The principal safety outcome was bleeding, which was subdivided into major and minor bleeding as defined by the studies.

Cost analysis in US\$ was based on figures from an actual trial of LMWH and standard heparin carried out at McMaster. It has, therefore, a distinct North American bias, but the cost inferences are probably valid for the British experience.

Studies

There were six studies involving over 1,400 patients. All required that patients were aged 40 years or more, three were double blind, four required patients to have had general anaesthesia and three used elastic stockings in combination with anticoagulant prophylaxis. In five studies the first dose of heparin was given intravenously.

Results

The only statistically significant differences found were for total DVT and proximal DVT. There were no differences for distal DVT or total, major or minor bleeding events.

LMWH resulted in a reduction of total DVT from 149 of 685 patients (22%) to 117 of 735 patients (16%; odds ratio 0.72, 95% CI 0.53 - 0.95) and of proximal DVT from 86 of 685 patients (13%) to 40 of 735 patients (5%; 0.40, 0.28 - 0.59).

Numbers-needed-to-treat

Combining the data, the numbers-needed-to-treat to prevent one episode of total DVT using LMWH compared with standard heparin was 17 (10 - 57) and to prevent one episode of proximal DVT was 14 (10 - 24).

Cost analysis

Analysis showed that proximal DVT increased hospital stay by 5 days. The cost analysis showed that this would add about \$1,400 to the total cost.

The relative cost of LMWH to standard heparin was an important factor in the cost analysis. If the relative cost of

LMWH was less than 3.7 times that of the standard heparin, the cost analysis favoured LMWH. However, based on the cost of managing 1,000 patients, when the ratio was between 2.6 and 5.0, the balance of costs was only about \$50,000 either way - some \$50 per patient. Only when the cost of LMWH was 10 times that of standard heparin was there a significant balance of cost in favour of standard heparin. In the UK, LMWH costs about 10 times more than standard heparin.

The cost analysis did not include the cost of managing recurrent DVT and the post thrombotic syndrome, two potentially important long-term complications of DVT. Inclusion of these factors in a cost analysis would favour the use of LMWH.

TREATMENT

LMWH in the initial treatment of DVT

Patients with DVT are at high risk of recurrent thromboembolic events (5 - 10% incidence), death in the months following the initial event and disabling chronic venous insufficiency in subsequent years. LMWH and standard unfractionated heparin have been compared in the treatment of established DVT. A meta-analysis has looked at results on over 2,000 patients in 16 RCTs [2].

Studies

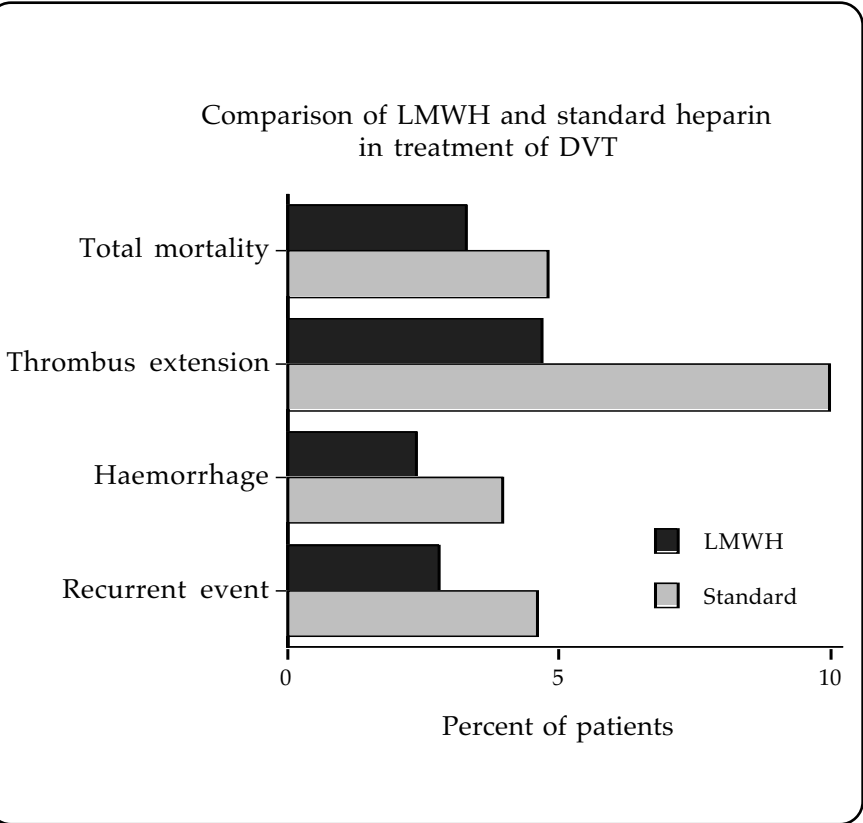
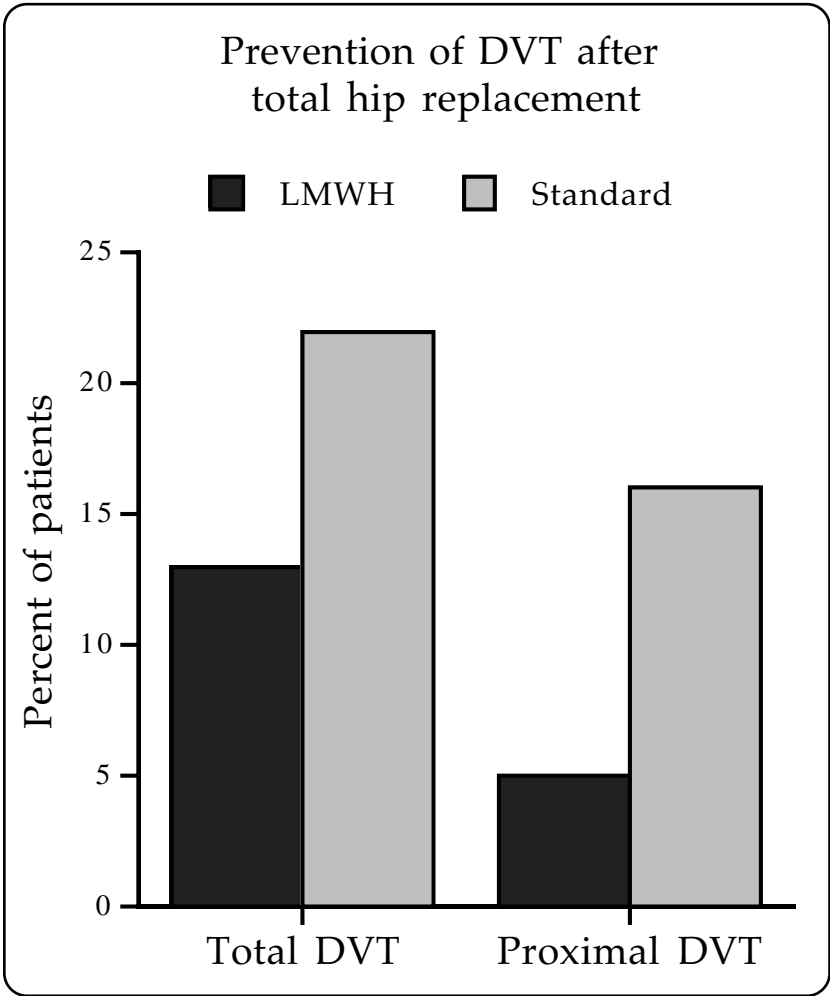
The 16 studies had a control group treated with standard unfractionated heparin and a treatment group with LMWH. Subcutaneous administration of LMWH was used in 14 studies, in 5 studies of standard heparin. Patient follow up in the studies varied from just the hospital stay to up to 23 months.

Outcomes

The outcomes sought were all recurrent thromboembolic events during the trial period (DVT of the legs and fatal or non-fatal pulmonary embolism), short term major haemorrhages, extension of the thrombus (by venography) and total mortality.

Results

There were non-significant reductions in total mortality, recurrent thromboembolic events and major bleeding associated with the use of LMWH. Significance was only achieved with thrombus extension which occurred with 28 of 597 patients treated with LMWH compared with 60 of 602 patients treated with standard heparin (odds ratio 0.51, 95% CI 0.32 to 0.83).



Numbers-needed-to-treat

Nineteen patients with established DVT would need to be treated with LMWH compared with standard heparin to **prevent** one incident of thrombus extension.

Venographically determined thrombus extension was the least clinically relevant of all the outcome measures used. The trend in favour of LMWH improving mortality, recurrent thromboembolic episodes or major haemorrhage was not statistically significant. The studies conducted to date were of low power to detect a significant difference; to demonstrate a reduction in mortality from 5% to 2.5% would need 2,500 patients. Since more studies with larger numbers are presently underway, it is entirely possible that LMWH will be shown to be more effective in due course.

References:

- 1 DR Anderson, BJ O'Brien, MN Levine, R Roberts, PS Wells, J Hirsh. Efficacy and cost of low-molecular-weight heparin compared with standard heparin for the prevention of deep vein thrombosis after total hip arthroplasty. *Annals of Internal Medicine* 1993 119: 1105-12.
- 2 A Leizorovicz, G Simonneau, H Decousus, JP Boissel. Comparison of efficacy and safety of low molecular weight heparin and unfractionated heparin in initial treatment of deep venous thrombosis: a meta-analysis. *British Medical Journal* 1994 309: 299-304.

DOES TREATING ACUTE HERPES ZOSTER IN PRIMARY CARE STOP POST HERPETIC NEURALGIA?

There is no consensus on how acute herpes zoster (shingles) should be managed in general practice. A particular problem is that patients with the disease go on to have persistent pain afterwards. It is thought that about 15% of patients have pain one month after healing of an acute herpetic rash, with about one quarter of these still have pain at one year.

This risk of postherpetic neuralgia increases with age. It can be as high as 50% in patients aged over 60 years and 75% in those aged over 75 years.

Treatment of the acute rash can include antiviral agents and corticosteroids. These have a cost (a week's treatment with acyclovir can cost over £100) and some adverse effects. Postherpetic neuralgia imposes a significant burden of suffering, and effective remedies that prevented postherpetic pain would be welcomed.

The question of whether treatments now used are effective is largely answered by a thorough systematic review and meta-analysis [1].

The study from Oxford and Flinders identified studies of the treatment of herpes zoster using standard searching

techniques. Twenty-one trials were identified in this way; they examined several treatments, including acyclovir, other antivirals and corticosteroids.

The main outcome sought was prevalence of pain at one, three and six months after onset of acute herpetic rash.

Acyclovir

Acyclovir was studied in eight trials with over 900 patients followed up who had received acyclovir for between five and ten days. At six months, 76 of 466 (16%) of patients receiving placebo had pain, compared with 61 of 455 (13%) of patients who received acyclovir.

No statistically significant reduction in pain was detected at one month (odds ratio 0.85, 95%CI 0.61 - 1.19) or six months (0.70, 0.47 - 1.06), but at three months there was a significant benefit (0.65, 0.46 - 0.93). Similar results were obtained for the studies which used only higher doses of acyclovir.

Other antivirals

These studies generally failed to demonstrate any differences at six months, or were of low numbers or quality, making conclusions suspect.

Corticosteroids

These were also of generally poor quality, and failed to show any significant differences.

How big is the effect

Remembering that there was no statistical difference between acyclovir and placebo, what would be the size of any effect if it were present but the studies were insufficiently large to demonstrate it? The best interpretation is that if acyclovir truly reduced the prevalence of postherpetic neuralgia by 30%, then 15 patients would have to receive a course of treatment to prevent one developing postherpetic neuralgia. To demonstrate an effect of 30% would need a study with over 1,500 patients.

The argument is not complex. Studies have been done which have had low power to detect even a relatively significant effect. Overall, the combined results in over 900 patients are not convincing. Getting a definitive answer would be long and costly, and the result even then would be likely to be clinically insignificant even if it were statistically significant.

Why bother?

With limited resources, the implication of all this is that different treatments should be explored.

Reference:

- 1 T Lancaster, C Silagy, S Gray. Primary care management of acute herpes zoster: systematic review of evidence from randomized controlled trials. *British Journal of General Practice* 1995 45: 39-45.

ARE AUTOLOGOUS BLOOD TRANSFUSIONS COST-EFFECTIVE?

Health care is full of hard decisions. Those decisions are often made harder by the glare of media attention, and an inadequate assessment of risk by patients and doctors. An example might be the patient who is awaiting an operation and has been concerned by the risk of blood-borne infection of hepatitis or HIV from blood transfusions.

The obvious answer is for the patient to donate his or her own blood before the operation, to be used during the operation - autologous blood transfusion. That would avoid the danger of infection, and nothing could be simpler.

Not quite, according to a study from Los Angeles published in the New England Journal of Medicine [1]. This report used a decision-analysis method to determine the cost-effectiveness of autologous transfusions for four different operations, total hip replacement, coronary artery bypass grafting, abdominal hysterectomy and transurethral prostatectomy.

Decision-analysis

The methods they used were essentially simple. What were the costs associated with autologous blood collection and transfusion - how much was actually used during the operation balanced against the cost of screening ordinary blood donations. What were the risks of developing hepatitis C or B or HIV or HTLV? How might the blood-borne acquisition of these viruses affect a patient's life in the years remaining, and so on. The details are fascinating for those wanting themselves to consider decision-analysis methods in other contexts.

Major determinants

What are the major determinants of costs and effectiveness?

First is the fact that not all of the autologous blood collected is used - 84% in the case of hip replacement, but only 4% for prostatectomy; the unused blood is almost always discarded rather than used for other patients.

Then there is the probability of catching something nasty from ordinary blood transfusions - pretty remote in Los Angeles, it would seem - with a 3 in 10,000 chance of getting hepatitis C, a 5 in 1,000,000 chance of getting hepatitis B and HIV.

Age is a factor - the more years of life remaining, the more chance there is that hepatitis or HIV will significantly affect that life - and most people having these operations will be in their sixth and seventh decades of life.

Results

So the result is that the cost is actually surprisingly high. The cost effectiveness of autologous blood transfusion for each quality-adjusted year of life (QALY) is some \$235,000 for hip-replacement, but 100 times more at \$24,000,000 for prostatectomy. Sensitivity analysis showed that however the case was argued, the cost was still high.

British experience?

These are US figures which do not always translate well to the British experience. Nevertheless, they offer an order-of-magnitude estimate of the actual costs of autologous transfusion programs, and provide a starting point for considering such a programme.

Reference:

- 1 J Etchason, L Petz, E Keeler et al. The cost effectiveness of preoperative autologous blood donations. New England Journal of Medicine 1995 332: 719-24.

Baseline calculations of cost-effectiveness for autologous blood transfusion in four operations

Variable	Total hip replacement	Coronary artery bypass	Abdominal hysterectomy	Transurethral prostatectomy
Mean age of patients (years)	62	67	49	68
Percent of blood used	84	72	26	4
Extra cost per unit transfused (\$)	68	107	594	4,783
Cost effectiveness (\$000/QALY)	235	494	1,358	23,643

“GOLD STANDARDS”

Once upon a time it was simple to distinguish effective from ineffective interventions. The “gold standard” for evaluation was a randomised controlled trial. To understand whether or not the result was statistically, and by implication, clinically significant one looked at the ‘p’ value - the probability that the result could have occurred by chance.

In more recent years the ‘p’ value has been complemented by confidence intervals. These indicate a range of values within which the true value is thought to lie. A 90% confidence interval indicates that the true value will lie in the indicated range nine times out of ten. A 95% confidence interval indicates that the true value will lie in the indicated range nineteen times out of twenty.

Even more recent studies of trial methodology indicate just how cautious one has to be in accepting results of randomised controlled trials, which, on the face of it, have an adequate trial design.

Quality counts in RCTs

Ken Schultz and his colleagues in the UK have reviewed the methodological quality of 250 controlled trials and related the quality of a trial, and in particular the process of randomisation, to the results [1]. Did inadequate design exaggerate the effect measured in the trial?

They compared trials in which the authors reported adequately concealed treatment allocations with those in which treatment allocation was either inadequate or unclearly described, as well as examining the effects of exclusions and double blinding.

The results were striking and sobering. As the table shows, the odds ratios were exaggerated by 41% in trials in which there was an inadequate concealment of treatment allocation, and by 30% when the process of concealing allocation was unclearly stated. Inadequate blinding also contributed to exaggerated odds ratios.

This is one of a series of superb analyses of trial design which leads inexorably to the conclusion that unless a trial is designed and *reported* to the highest standard, then its results must be treated with a degree of caution. Librarians might consider ensuring that key references from this article are immediately on hand.

Structured Reporting of RCTs

What is the highest standard? A proposal for structured reporting of randomised controlled trials was set out some months ago [2]. It is detailed and sensible. It may stretch the mind to ensure that all of its many recommendations are adhered to, but those who write reports of trials and edit medical journals would do well to consider it in detail.

Perhaps in future looking for RCTs will be replaced by looking for ACTACTs - adequately concealed treatment allocation controlled trials.

References:

- 1 KF Schultz, I Chalmers, RJ Hayes, DG Altman. Empirical evidence of bias: Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *Journal of the American Medical Association* 1995 273: 408-12.
- 2 Standards of Reporting Trials Group. A proposal for structured reporting of randomized controlled trials. *Journal of the American Medical Association* 1994 272: 1926-31.

Methodological Quality and Estimates of Treatment Effects in Controlled Trials

Methodological Issue

Exaggeration of Odds Ratio (%)

Inadequate method of treatment allocation

larger by 41%

Unclear method of treatment allocation

larger by 30%

Trials not double blind

larger by 17%

Participants excluded after randomisation

no effect

Trials were compared with those with adequately concealed treatment allocation

THE MUST-READ TRIAL

Every so often comes along a trial report which comes into the “must-read” category. It can be a super design, or an important result, or often both.

One such is the recent Lancet report of the Collaborative Eclampsia trial from Lelia Duley [1].

How big is the problem?

Eclampsia is the occurrence of one or more convulsions in association with the syndrome of pre-eclampsia. It is relatively uncommon in developed countries where it complicates about one in every 2,000 deliveries. Eclampsia can be 20 times more common in developing countries, and it probably accounts for more than 50,000 maternal deaths worldwide each year.

What is the question?

What should be used to treat the convulsions? Diazepam, phenytoin and magnesium sulphate have and are being used.

The Collaborative Eclampsia Trial was set up to determine which, if any, is superior. There were nearly 1,700 women randomised to treatments in two separate trials - magnesium sulphate against diazepam and magnesium sulphate against phenytoin.

For the trial of magnesium sulphate against diazepam 910 women were randomised in 23 centres in eight countries - Argentina, Brazil, Colombia, Ghana, India, Uganda, Venezuela and Zimbabwe. For the trial of magnesium sulphate against phenytoin 777 women were randomised in four centres in South Africa and India.

All women with a clinical diagnosis of eclampsia were eligible, with the only exclusions was if a study drug was contraindicated.

Treatments

Magnesium sulphate was given as an intravenous loading dose followed by intravenous infusion or intramuscular injections for 24 hours. Diazepam was given as an intravenous loading dose followed by an intravenous infusion for 24 hours. Phenytoin was given as a slow intravenous infusion followed by further intravenous doses every six hours for 24 hours.

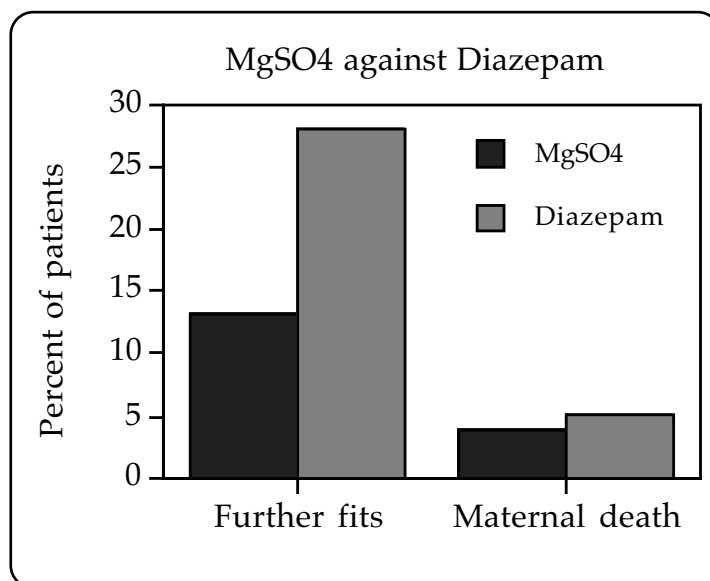
Outcomes

The primary outcomes were recurrence of convulsions and maternal death. There were other secondary outcomes - though these are not commented on here.

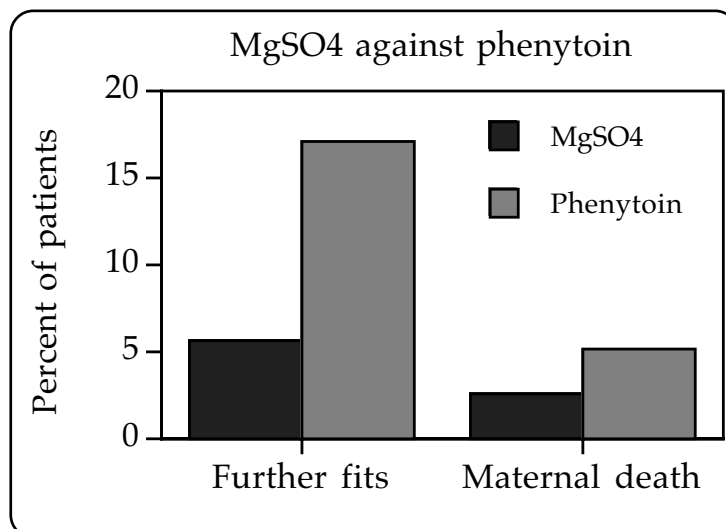
Results

Magnesium sulphate was superior to diazepam; significantly fewer recurrences of fits occurred with magnesium

sulphate (60/453) than with diazepam (126/452). The relative risk was 0.48 (95%CI 0.4 - 0.6). The reduction in maternal death (17/453 compared with 23/452) was not significant.



Magnesium sulphate was superior to phenytoin; significantly fewer recurrences of fits occurred with magnesium sulphate (22/388) than with diazepam (66/387). The relative risk was 0.33 (95%CI 0.2 - 0.5). The reduction in maternal death (10/388 compared with 20/387) was not significant.



Numbers-needed-to-treat

This was a comparison of medicines which were thought to be effective - but asking the question which was best. The NNT for magnesium sulphate against diazepam was 7 (5 - 11). The NNT for magnesium sulphate against phenytoin was 9 (6 - 14). Thus treating every eight women with eclampsia with magnesium sulphate rather than diazepam or phenytoin results in one fewer case of recurrent fits.

Conclusions

To conduct a large multicentre study across three continents, and to do it so beautifully, is a rare event. To do it well, and to produce such clear cut results, is exceptional. This is a classic study - and one to treasure.

Reference:

L Duley. Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. Lancet 1995 345: 1455-63.

THE ANTI-WEASEL CAMPAIGN: GREYNESS, NNTs AND LIFE

The greyness of medicine upsets managerial talent - why do we always have to add so many caveats to our guidelines? Reality is that clinical decisions are necessarily context-dependent. Nonetheless we need ways to encapsulate the evidence from RCTs and systematic reviews, ways which are useful in making both clinical and policy decisions, and which make the context explicit. Numbers-needed-to-treat (NNT) is Bandolier's current favourite encapsulating tool (see #11 [Jan 95] on), and readers have asked for a how-to-do-it repeat.

The example is taken from a survey of the risk that epidurals in childbirth are associated with an increased risk of long term back problems [1]. Long term back problems after:

The example is not from RCT data, and so should carry a greyness warning that it may be incorrect. Bandolier uses it because it is a lovely example of the greyness - when is the data true? - and, more importantly, because childbirth groups use it in their literature and the professionals have

no epidural	epidural	NNT	95%CI
47/403	109/612	16.3	9.5 - 56

$$NNT = \frac{1}{(109 / 612) - (47 / 403)}$$

to answer it, optimally by doing the RCT to rebut the allegation, difficult though this may be.

The current professional argument is that women with more difficult labours are more likely to have epidurals. The difficult labours are themselves more likely to result in long term back problems.

References:

- 1 RJ Cook, DL Sackett. The number needed to treat: a clinically useful measure of treatment effect. British Medical Journal 1995 310: 452-4.
- 2 R Russell, P Groves, N Taub, J O'Dowd, F Reynolds. Assessing long term backache after childbirth. British Medical Journal 1993 306: 1299-1303.

NNTs FOR CARDIAC INTERVENTIONS

These are NNTs for a variety of cardiac interventions from some of the major trials published in recent years that *Bandolier* has found useful. They are reproduced here with a simple health warning - that readers should always go back to original papers to get all the nuances of the original studies.

Intervention	Outcome	NNT
Myocardial Infarction		
streptokinase alone (vs. nothing) ISIS2	prevent 1 death at 5 weeks	40
aspirin alone (vs. nothing) ISIS2	prevent 1 death at 5 weeks	40
streptokinase + aspirin (vs. nothing) ISIS2	prevent 1 death at 5 weeks	20
tPA	haemorrhagic stroke	500
streptokinase	haemorrhagic stroke	1000
tPA vs streptokinase (GUSTO)	save 1 life with tPA vs. streptokinase	100
thrombolytic therapy 5 hr earlier	save 1 life	100
Heart Failure		
enalapril in Class IV CHF (NYHA)	prevent 1 death at 1 year	6
enalapril in Class I or II CHF (NYHA)	prevent 1 death at 1 year	100
Others		
CABG in left main stenosis	prevent 1 death at 2 years	6
carotid endarterectomy in highgrade symptomatic stenosis	prevent 1 stroke or death in 2 years	9
simple antihypertensives for severe hypertension	prevent 1 stroke, MI or death in 1 year	15
simple antihypertensives for mild hypertension	prevent 1 stroke, MI or death in 1 year	700
aspirin in unstable angina	prevent MI or death in 1 year	25
aspirin in healthy US physician	prevent MI or death in 1 year	500
treating hypertension in the over-60s	prevent 1 coronary event	18
simvastatin vs. placebo in CHD	prevent 1 coronary death over 5 years	29
simvastatin vs. placebo in CHD	prevent 1 major coronary event over 5 years	15

DESERT ISLAND TEXT

Lewis Thomas is a man of whom our editor would approve. His writings more than amply show that "he thinks the unthinkable, questions the unquestionable and is in addition thoroughly interesting. Moreover he has a Welsh background (admittedly several generations distant - see *Bandolier* #10).

Lewis Thomas would be my chosen companion on the desert island to which *Bandolier* has consigned me. To explain why, I don't think I can do better than pass on the *Washington Post's* advice on Thomas' first book, "The Lives of a Cell" - "read this book....ponder it, read it again, for it is an unlikely, indeed a rare work, an ode to biology, luminous in style and bursting with information, a celebration of, and a cerebration on life, and intensely interesting". *Time* simply described Thomas as "quite possibly the best essayist on science now working anywhere in the world".

The attributes that would be so valuable on the island are the originality of Thomas' ideas, his unexpected interpretations of apparently ordinary phenomena and the amazing breadth of his writing. As a research scientist Lewis Thomas made an impact by suggesting that an immunosurveillance mechanism protects us from the possible ravages of mutant cells, an idea later championed by Macfarlane Burnett. I have always had a soft spot for the concept of immunosurveillance, since like the Emperor's new clothes it neatly explains the absence of something that has never been shown to exist! Thomas also proposed that viruses have played a major rôle in the evolution of species by their ability to move pieces of DNA from one individual or species to another.

As physician, medical educator and administrator Thomas is well qualified for the rôle of elder statesman and philosopher. As an essayist he has a knack of delighting his readers, surprising them and then perhaps humbling or deflating them. One is never sure what is coming next even though you think you know the subject. The titles of the essays are an entertainment in themselves and they encourage speculation on what might be forthcoming: the corner of the eye; the attic of the brain; the scrambler in the mind; on etymons and hybrids; on transcendental metaworry; the youngest and brightest thing around; late night thoughts on Mahler's ninth symphony; notes on punctuation (oh dear!); the wonderful mistake (if DNA had replicated perfectly there might be no evolution - but what about the viruses?). There is something here for everyone and I challenge readers not to be stimulated by Lewis Thomas' writing.

There seems to be a developing tendency amongst contributors to this column to stretch the (imaginary) rules and I propose to extend this by imagining a 'collected works' of Thomas. After all he has only (to my knowledge) published five slim volumes of essays and one autobiographical volume, apart, of course, from his scientific and medical papers. These could easily be contained within one cover. This volume would contain something over one hundred essays.

The ration could be one a day or one a week. For how long has *Bandolier* abandoned me? Is a rescue planned in a few months (one a day); a couple of years (one a week) or never (the essays can stand re-reading many times).

Dr Eric Sidebottom
Oxford

Lives of a cell. 1974, Allen Lane
The Medusa and the Snail. 1980, Allen Lane
The Youngest Science. 1983, Oxford University Press
Late Night Thoughts. 1984, Oxford University Press
The Fragile Species. 1993, Collier (Macmillan)

STOCKING FILLERS

TACKLING INEQUALITIES IN HEALTH

edited by Benzeval, Judge & Whitehead. King's Fund, London 1995. pp140 £14.95 ISBN 1 85717 088 1

Bandolier touched on social inequalities in health (#6) and has now found a book which gathers together the evidence that poverty shortens your life. Unfortunately the remedies by and large fall outside the provision of health care. Like many current nightmares - who will have jobs in 2010? who will pay the pensions in 2010? - the poverty/health trap is a huge policy problem for any thinking government in the developed world.

The obligations of a health care system are "to ensure equity of access, distributing resource in relation to need", and to keep trumpeting that the inequalities are large and growing. The targets proposed may not be novel - they include neglected population groups (women, older people, minority ethnic groups), education, unemployment and child care provision - and the taxation solutions may not be palatable, but can we afford to take no action? Recommended.

WHERE TO BE BORN?

Rona Campbell & Alison Macfarlane. National Perinatal Epidemiology Unit, Oxford, 2nd edition 1994. pp170 £7.00 ISBN 0-9512405-1-x.

Who do you think might have said "our only resource at present is to deal with such statistical information as we possess and to ascertain fairly what it tells us". The answer is Florence Nightingale, over 100 years ago. The authors of this review, the second edition of a book first published eight years ago, have tried to follow this principle.

They certainly give lots of information woven into a fascinating perspective, both historical and contemporary, of the making of policy about where to be born. An eye opening read, well worth £7, and deserving of a place on the bookshelf.